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(54) Title: FORMULATIONS USEFUL AGAINST HEPATITIS C VIRUS INFECTIONS

(57) Abstract: The present invention relates generally to chemical compounds and substances which are effective against Hepatitis C virus (HCV) infections. Moreover, the present invention relates to compositions comprising said compounds and/or substances, to methods for preventing HCV infections as well as use of the compounds and/or substances for the preparation of compositions useful for the prophylaxis and/or treatment of HCV infections. Useful compounds and substances according to the invention are selenium, selenium salts, Vitamin D₃ and retinoids, like all trans retinoic acid and salts thereof, C₁ - C alkyl amide of all trans retinoic acid and salts thereof, C₁ - C₁₀ alkyl esters of all trans retinoic acid and salts thereof, 9-cis retinoic acid and salts thereof, C₁ - C₁₀ alkyl amide of 9-cis retinoic acid and salts thereof, C₁ - C₁₀ alkyl esters of 9-cis retinoic acid and salts thereof, (E)-4-[2 (5,6,7,8-tetrahydro-5,5,8,8-tetra methyl-2-naphthalenyl-1-propenyl) benzoic acid (TTNPB), (4-[5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl] carboxamido) benzoic acid (AM-580), N-(4-hydroxyphenyl) retinamide (4-HPR), and 6-[3-(1-adamantyl) 4-hydroxyphenyl]-2-naphthalene carboxylic acid (AHPN).

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K33/04 A61P31/14 A61K31/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, EMBASE, CHEM ABS Data, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 02/084294 A (AXXIMA PHARMACEUTICALS AG ; HERGET THOMAS (DE); COTTEN MATTHEW (DE)) 24 October 2002 (2002-10-24) cited in the application the whole document page 5, line 8 - line 17 page 6, line 14 - line 17 page 7, line 25 - line 37 page 11, line 11 - line 22 page 12, line 28 - line 43</p> <p>-----</p> <p>-/-</p>	1-50

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- °A° document defining the general state of the art which is not considered to be of particular relevance
- °E° earlier document but published on or after the International filing date
- °L° document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- °O° document referring to an oral disclosure, use, exhibition or other means
- °P° document published prior to the international filing date but later than the priority date claimed

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- °X° document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- °Y° document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- °&° document member of the same patent family

Date of the actual completion of the international search 2 July 2004	Date of mailing of the international search report 14.07.2004
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Authorized officer Economou, D

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LOOK M P ET AL: "Interferon/antioxidant combination therapy for chronic hepatitis C-A controlled pilot trial" ANTIVIRAL RESEARCH, ELSEVIER SCIENCE BV., AMSTERDAM, NL, vol. 43, no. 2, 1999, pages 113-122, XP002232553 ISSN: 0166-3542 the whole document abstract page 115, right-hand column, line 2 - line 3 -----	1-50
X	DE 43 20 878 A (LESKOVAR PETER DR DR HABIL) 26 January 1995 (1995-01-26) column 40, line 61 - line 62 -----	1, 4, 7, 8, 19
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X	WO 02/066022 A (WILLIAMS ANTHONY H; ARONEX PHARMACEUTICALS INC) 29 August 2002 (2002-08-29) cited in the application the whole document page 1, lines 3-7 page 3, line 19 - page 6, line 2 page 8, line 3 - line 6 examples 1,2 page 13, line 3 - line 14 -----	1-3, 5-11, 13-29, 31-50
X	WO 97/03682 A (CIRD ; FONTANA JOSEPH A (US)) 6 February 1997 (1997-02-06) page 19, line 24 - page 24, line 15 claims 14,15,17,21 -----	1-3, 5-8, 19, 20
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X	DE 36 10 531 A (MCNEILAB INC) 16 October 1986 (1986-10-16) claims 1-11 the whole document -----	1, 7, 8, 19
		-/-

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/32413 A (LIM SOO JEONG ; LOPEZ BERESTEIN GABRIEL (US); TARI ANA M (US); UNIV TE) 25 April 2002 (2002-04-25) page 11, line 1 - page 25, line 10 page 75, line 13 - line 22 page 78, line 4 - page 81, line 20 example 4 -----	1-3,5-8, 19
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X	DE 199 36 672 A (HERMES FABRIK PHARM PRAEPARATE) 15 February 2001 (2001-02-15) the whole document -----	1-3, 5-11, 13-29, 31-50
P,X	US 2003/180719 A1 (HERGET THOMAS ET AL) 25 September 2003 (2003-09-25) the whole document -----	1-50

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International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-3,5-11,13-29,31-50 (all partially), 4,12,30

Compositions comprising selenium or selenium salts (1-8, 19-20), their use for the manufacture of a medicament for the treatment or prophylaxis of hepatitis C infections (claims 9-18,28-35), corresponding methods in-vivo and in-vitro (claims 21-27,36-41) and methods for regulating the expression and activity of the human cellular protein peroxidase-gastrointestinal in-vivo and in-vitro (42-50).

2. claims: 1-3,5-11,13-29,31-50 (all partially)

Compositions comprising Vitamin D3 (1-3, 5-8,19-20), their use for the manufacture of a medicament for the treatment or prophylaxis of hepatitis C infections (claims 9-11,13-18, 28-29, 31-35), corresponding methods in-vivo and in-vitro (claims 21-27,36-41) and methods for regulating the expression and activity of the human cellular protein peroxidase-gastrointestinal in-vivo and in-vitro (42-50).

3. claims: 1-3, 5-11, 13-29, 31-50 (all partially)

Compositions comprising all trans retinoic acid, derivatives thereof and 4-HPR (1-3, 5-8,19-20), their use for the manufacture of a medicament for the treatment or prophylaxis of hepatitis C infections (claims 9-11,13-18, 28-29, 31-35), corresponding methods in-vivo and in-vitro (claims 21-27,36-41) and methods for regulating the expression and activity of the human cellular protein peroxidase-gastrointestinal in-vivo and in-vitro (42-50).

4. claims: 1-3, 5-11, 13-29, 31-50 (all partially)

Compositions comprising the naphthalene derivatives TTNPB, AM-580 and AHPN (1-3, 5-8,19-20), their use for the manufacture of a medicament for the treatment or prophylaxis of hepatitis C infections (claims 9-11,13-18, 28-29, 31-35), corresponding methods in-vivo and in-vitro (claims 21-27,36-41) and methods for regulating the expression and activity of the human cellular protein peroxidase-gastrointestinal in-vivo and in-vitro (42-50).

INTERNATIONAL SEARCH REPORT

Information on patent family members

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